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(71) Applicant
Robert Henry Abplanalp
10 Hewitt Avenue, Bronxville, New York 10708,
United States of America

(72) Inventor
Robert Henry Abplanalp

(74) Agent and/or Address for Service
D Young & Co
10 Staple Inn, London, WC1V 7RD, United Kingdom

(54) Sterilizing valved pressure containers

(57) A valved pressure, e.g. aerosol, container, is sterilized by sealing therein an aqueous saline solution under superatmospheric pressure, the solution having been subjected to electrolytic action. The solution may be released from the container to clear contact lenses.

A VALVED PRESSURE CONTAINER
HAVING AN AQUEOUS SALINE SOLUTION THEREIN
AND A METHOD FOR STERILIZING THE CONTAINER

5 The present invention relates to a valved pressure container containing a saline solution, and to a method of sterilizing such a container.

10 Isotonic saline solutions are used, for example, in the washing and cleaning of "soft" contact lenses. The isotonic saline solution, in one form, is packed into an aerosol container with a suitable propellant. The solution is then dispensed onto the contact lens when the lens needs cleaning. It is essential that the aerosol saline product be free of bacteria.

15 To ensure freedom from bacteria, the industry presently packs the saline solution and propellant into a sealed aerosol container having a manually actuatable valve disposed in the container opening. After the aerosol unit is formed, the entire unit is then transported to a suitable radiation facility and the entire unit is radiated. This operation is costly.

Moreover, subsequent to the radiation treatment, the saline solution of the aerosol unit does not possess residual bacteria killing or bacteria controlling activity.

The lack of bactericidal or bacteriostatic activity in an isotonic saline solution that has been sterilized by radiation creates a particular problem in that said solution cannot sterilize "soft" contact lens. "Soft" lens, which normally consists of a copolymer of mainly a hydrophilic monomer, such as a 2-hydroxy ethyl methacrylate, have approximately thirty percent (30%) by weight of water, or more, and thus the lens itself offers a vehicle or environment suitable for the propagation of various kinds of bacteria. The use of bacteria contaminated contact lens may cause serious injury to the human oculus tissue.

Therefore, as a method for sterilizing a water-containing contact lens ("soft" lens), there has been proposed a method of boiling the lens for a predetermined period of time. Although this method is very effective for sterilization, it has, at the same time, the following defects. That is:

(1) the protein in lachrymal liquid adhered to the lens due to boiling comes to fix to the surface of the lens as it is thermally degenerated, which not only spoils the optical property of the lens but also makes the lens feel very uncomfortable when in place in the eye.

(2) The slightly cross-linked hydrophilic copolymer of 2-hydroxyethyl methacrylate material for the water-containing contact lens deteriorates by the repeated boiling treatments so that the lens becomes discolored or the rated configuration

thereof changes to greatly shorten the life of the lens.

(3) Due to the use of an AC power source on a boiling heater, it is inconvenient for one to carry the sterilizer in travel and especially, when one is in an outdoor environment such as a camp site or the like, the sterilizer can not be used because no power source is available there.

(4) Non-water-containing contact lens made of polyethyl methacrylate or silicon rubber are not suitable for boiling sterilization.

As a means for overcoming such difficulties involved in the boiling sterilization, there has been proposed a method for sterilizing a contact lens with various kind of sterilizing liquid medicines like thimerosal or chlorhexidine. However, such method has its drawbacks in that due to the molecular spacing in the structure of the water-containing contact lens, the sterilizing component in the sterilizing liquid medicine tends to be absorbed into the lens and cause an anaphylactic inflammation of the oculus tissue.

Beside the above method, there has also been a prior method in which the lens is sterilized with a 3% sodium hydrogen peroxide solution and a catalyst such as platinum is brought into contact with the solution to decompose the sodium hydrogen peroxide into water and oxygen so that the lens is made sterile. However, this method has also had drawbacks in that a long time is required for sterilization and the process is complicated and impractical.

We have now found it possible to provide a method for sterilizing a saline _____

solution; for example an isotonic saline solution; and the resultant sterilized saline solution in an aerosol container, which method and product avoid the drawbacks of the prior art.

We have also found it possible to provide an isotonic saline solution
5 having residual bactericidal and/or bacteriostatic properties.

In one aspect, the invention provides a valved pressure container having an aqueous saline solution under superatmospheric pressure stored therein, said saline solution having been subjected to electrolytic action to effect a sterilization of the saline solution and consequent sterilization of
10 inner surfaces of the container and any other products stored within the container.

In another aspect, the invention provides a method for sterilizing an aerosol container comprising sealing in the container under superatmospheric pressure a saline solution that has been subjected to electrolytic
15 action.

Various preferred features and embodiments of the invention are described below.

The subject invention, in one aspect, comprises an efficient method for sterilizing a sealed container having an aqueous saline solution as at
20 least one component thereof. In one form, a saline solution is electrolyzed in an electrolytic cell and sealed in an aerosol container with a valve-bearing mounting cup and then pressure filled with propellant. In a more specific form of this aspect, the isotonic saline solution is the saline solution.

In another aspect the invention comprises a sealed pressurized saline solution having bactericidal and/or bacteriostatic activity, said active saline solution being generated by subjecting the saline solution to electrolysis. In the preferred form, the saline solution, more preferably an isotonic saline solution, is passed through an electrolytic cell immediately prior to entering
30 the pressurized (aerosol) container, the container is then closed with a closure (mounting cup) bearing a manually actuatable valve, and the container pressure filled with propellant.

The invention will be hereafter described with reference to an isotonic saline solution (0.9% NaCl).

The electrolytic cell useful in sterilizing the isotonic saline solution is not part of this invention. Such a cell is described in complete detail in United States Patent No. 3,443,055 issued 6th May, 1969; the disclosure of
35 United States Patent —————

No. 3,443,055 being incorporated into and made a part of the subject disclosure. Also incorporated into the subject disclosure is United States Patent No. 3,616,355 showing a method of generating enhanced biocidal activity in the electrolysis of chloride containing solutions at higher voltages than those disclosed in the '055 patent.

Other electrolytic cells suitable for sterilizing the isotonic saline solution are described in United States Patent Nos. 3,479,275 and 3,547,600.

In packaging the isotonic saline solution in an aerosol container, and in the preferred form, the saline solution is flowed through a suitable electrolytic cell and into a contiguous aerosol container and the container sealed by crimping a closure (mounting cup) bearing a manually-actuatable valve onto the open end or bead of the container. The container is then pressure filled with propellant.

It has been found that flowing an isotonic saline solution through electrode plates under the following conditions and parameters produced a product having the capability of sterilizing the saline solution and the inner surfaces of an aerosol container and other components in the container. These containers further produced saline solution having bactericidal/bacteriostatic properties over a protacted period. The conditions and parameters are:

One thousand milimeters (ml) (1000 ml) of an isotonic saline solution was passed into an electrolytic cell wherein the electrodes were spaced two hundred seventy thousands of an inch (.270") apart. The facing surfaces of the electrodes were three (3) by two (2) inches. An electric charge of 7.8 volts and 5.0 amps was applied to the electrolytic cell and the saline solution released from the cell at the average rate of 35 seconds. The samples

discussed hereafter had two passes through the electrolytic cell unless otherwise noted.

The experimental data supporting the aforesaid statement regarding bactericidal/bacteriostatic activity are set forth hereafter.

Solutions of sodium chloride in distilled water (isotonic saline solution) were prepared and treated in several different ways before being packaged in an aerosol container fitted with an aerosol valve. Several different microorganisms were used in this study and each strain of microorganism was added to a different container of saline solution. Some of the solutions were then passed through an electrolytic cell and packaged into aerosol containers. Samples from each can were sprayed immediately after filling into the aerosol container and plated onto agar media. The plates were observed for bacterial growth after 24, 48 and 72 hours. Stored samples were also sprayed onto additional agar media and observed according to the above time schedule. Additionally, samples which were originally contaminated with microorganisms and found to be sterile after passing through the electrolytic cell were re-contaminated with microorganisms after standing about three (3) weeks. These were then sprayed as above and according to the same schedule.

The results obtained to date indicate the following:

1. Isotonic saline solution will support the growth of microorganisms.
2. Isotonic saline solution packaged in an aerosol container will maintain sterility if the product is initially sterile.
3. Isotonic saline solution containing microorganisms can be sterilized by passing the solution through an electrolytic cell.

4. Isotonic saline solution passed through an electrolytic cell, and added to an aerosol can containing microorganisms, is capable of killing the microorganisms and rendering the solution, can, valve and nitrogen propellant sterile.
5. After about three (3) weeks microorganisms were added to an aerosol can filled with sterile saline solution which had previously been passed through the electrolytical cell. The microorganisms were killed within a 24 hour period.

Experimental

I. Preparation of Saline Solutions (0.9% w/v)

A. Formulation

All solutions were prepared by taking 9.0 grams of Sodium Chloride, U.S.P. and adding it to sufficient distilled water to make 1000 ml. of solution. This is what is referred to as isotonic saline solution and is the type of solution used in the non-preserved contact lens cleaning solutions. Saline solutions prepared in this manner were used in this study.

B. Packaging

All aerosols were prepared by adding 200 ml. of the saline solution (treated or non-treated) to an aluminum aerosol container (Peerless Tube - 2.089" X 6 1/2" - #203 internally lined) and sealing the can with a Precision Valve (-0.018 Stem X 0.018" Body). Nitrogen gas was then added to the filled container at a pressure of 100 psig. A suitable actuator was then added to the valve.

C. Microorganisms Used

The following microorganisms were used in this study:

1. Escherichia Coli - is a gram-negative non-spore forming bacillus. It is found as normal flora in the intestinal tract. Some pathogenic strains of E. Coli have the ability to invade the intestinal mucosa and produce enterotoxins. The symptoms seen are fever, chills, abdominal pain and dysentery.
 - The bacteria grows very well on MacConkey agar and nutrient agar (pink colonies observed).
 - The bacteria grows best at an incubation 35-37°C.
 - The bacteria grows well in a saline environment.
 - One could observe growth within a 24-48 hour period.
2. Pseudomonas Aeruginosa - is a gram-negative obligate aerobe rod. It is commonly found in soil, water, sewage and (in a small percentage) in the intestinal tract.
 - The bacteria grows well on MacConkey agar and nutrient agar. The organism is known to produce a bluish pigment named pyocyanin and a greenish fluorescent pigment known as fluorescein.
 - The bacteria grows best at an incubation of 35-37°C and grows well in a saline environment. Growth was observed within a 48-72 hour period.

These organisms are opportunistic, infecting individuals who are debilitated, burned or immunosuppressed.

3. Salmonella - This organism is commonly found in spoiled foods and is responsible for food poisoning.

D. Media Used

Two types of media were used to determine if bacterial growth was taking place. When no growth was noted, then the product was deemed to be sterile. Petri dishes containing the appropriate growth media were sprayed with the saline solution which had been treated in different ways. The following types of media were used:

- A. MacConkey Agar was used to enhance the growth of gram-negative bacteria.
- B. Columbia CNA Agar was used to enhance the growth of gram-positive bacteria.

II. Results

The following combinations of saline solution, microorganisms and treatment through the electrolytic cell were studied to date:

- A. Non-treated Saline Solution (Control)
- B. Non-treated Saline Solution + Microorganism
- C. Saline Solution + Electrolytic Cell
- D. Saline Solution + Microorganism + Electrolytic Cell
- E. Saline Solution + Electrolytic Cell + Aerosol
Can Contaminated with Microorganisms

Tables I and II indicate the results obtained to date.

TABLE I
Sterility of Saline Solution (0.9%)

Treatment	Organism Added		Electrolytic Cell	MacConkey Media	CNA Media	Microbial Growth* 37°C			
	To Solution	To Tan				24 hrs	40 hrs	72 hrs	Repeat
Distilled Water	-----	-----	NO	YES	YES	NG	NG	NG	NG
Saline Solution (Non-Aerosol)	-----	-----	NO	YES	YES	NG	NG	NG	NG
Saline Solution (Non-Aerosol)	-----	-----	YES	YES	YES	NG	NG	NG	NG
Saline Solution (Aerosol)	-----	-----	NO	YES	YES	NG	NG	NG	NG
Saline Solution (Aerosol)	-----	-----	YES	YES	YES	NG	NG	NG	NG

NG = No Growth

*Even though no growth was noted, this is not an indication that growth will not occur if organisms are present. It just happened that no organisms were present in these samples.

TABLE II

Sterility of Saline Solution (0.9%) - With Microorganisms Added

Treatment	Organism Added		Electro-Lytic Cell	MacConkey Media	CNA Media	Microbial Growth 37°C:			
	To Solution	To Can				24 hrs	48 hrs	72 hrs	Repear after 3 weeks
Saline Solution (Aerosol)	E. Coli	---				+++	+++	+++	+++
Saline Solution (Aerosol)	E. Coli	---				NG	NG	NG	NG
Saline Solution (Aerosol)	---	---				YES	YES	+++	+++
Saline Solution (Aerosol)	---	---				YES	YES	+++	+++
Saline Solution (Aerosol)	B. Coli	NO				YES	YES	+++	+++
Saline Solution (Aerosol)	B. Coli	YES				YES	YES	+++	+++
Saline Solution (Aerosol)	Pseudomonas	NO				YES	YES	+++	+++
Saline Solution (Aerosol)	Pseudomonas	YES				YES	YES	+++	+++
Saline Solution (Aerosol)	---	---				NO	NG	NG	NG
Saline Solution (Aerosol)	---	---				YES	YES	+++	+++
Saline Solution (Aerosol)	---	---				YES	YES	+++	+++
Saline Solution (Aerosol)	Salmonella	NO				YES	YES	+++	+++
Saline Solution (Aerosol)	Salmonella	YES				YES	YES	+++	+++
Saline Solution (Aerosol)	---	---				NO	NG	NG	NG
Saline Solution (Aerosol)	Salmonella	NO				YES	YES	+++	+++
Saline Solution (Aerosol)	Salmonella	YES				YES	YES	+++	+++

+++ = Abundant Growth

NG = No Growth

Streptococcus F alkalies were also studied in a manner similar to the other organisms. Samples of organism were added to isotonic saline solution packages in an aerosol can. The samples packaged without passing through the electrolytic cell showed a great amount of bacterial growth while the samples passed through the cell and then packaged in an aerosol container showed no signs of growth.

The bactericidal/bacteriostatic properties of the isotonic saline solution is believed to be attributable to the formation of a combination of ozone, hydrogen peroxide and sodium hypochlorite.

In the past, passing saline solution through an electrolytic cell has produced a solution having a short time span of sterilization capability. However, it was unexpected to discover that saline solution passed through an electrolytic cell and promptly packaged in a pressurized vessel, such as an aerosol container, would retain the sterilization capability over a protracted period. Samples prepared according to the above have been found to retain their sterilization capability for a period approaching four months.

Chemical and Physical Studies

Drops in NaCl Content After Electrolysis

NaCl First Day <u>/ml</u>	ml Ag	mg NaCl	ml Ag	mg NaCl	ml Ag	mg No ₃ / ml No ₃
Not treated	15.62	9.1225	15.60	9.1196	15.70	9.1450
	15.60		15.61		15.60	
Passed	15.40	9.0290	15.35	8.9705	15.30	8.9296

Through Cell	15.50		15.35		15.26
2nd Day	15.40	8.9998	15.30	9.2050	15.22
	15.40		15.30		8.9004
6th Day	15.35	8.9559	15.30	8.9267	15.20
	15.30		15.25		8.8829
12th Day	15.35	8.9764	15.23	8.9121	15.20
	15.37		15.27		8.8887
18th Day	15.37	8.9822	15.21	8.9033	15.20
	15.37		15.26		8.8829
24th Day	15.36	8.9822	15.24	8.9121	15.20
	15.36		15.26		8.8829

The drop in sodium chloride content is consistent with the formation of sodium hypochlorite. The sterilization capability is affected by the duration of time that the saline solution is subjected to electrolysis; also suggesting that an increase in voltage may also affect the sterilization capability.

This is demonstrated by the following data:

	<u>Can #1</u>	<u>Can #2</u>	<u>Average</u>
Before Cell	9.0465	9.0407	9.0436
After 1 Pass	8.9413	8.9413	8.9413
2 Passes	8.8829	8.8946	8.8887
3 Passes	8.8595	8.8712	8.8654
4 Passes	8.8244	8.8303	8.8274
6 Passes	8.7660	8.7660	8.7660
10 Passes	8.6900	8.6783	8.6842

While the method of the invention has been described in terms of "electrolyzing" the saline solution outside the aerosol container, it should be understood that the pressure (aerosol) container, per se, may function as an electrolytic cell by the appropriate disposition of electrodes and electrical connection as part of the container.

Further, the method of the invention has been specifically described with reference to nitrogen as the propellant. Other propellants, both liquified gas and compressed gas may be utilized. In this connection, the method has been described in terms of adding propellant through pressure filling nitrogen gas. However, if other than compressed gases are employed as the propellant, other systems, such as, for example, under-the-cup filling of propellant may be employed.

Additionally, while the invention has been illustrated by describing an aerosol container wherein the propellant is disposed in the container in contact with the saline solution, it should be understood (and it is presently viewed by the inventor to be the best form for an aerosol container having sterilized saline solution) that the saline solution may be packed in an aerosol container of the so-called "piston" type. In the "piston" type aerosol container, the product to be dispensed and the propellant are separated by a piston which moves along the longitudinal axis of the container in response to the pressure generated by the propellant on one side of the piston. Actuation of the valve on the product side of the piston provides an opening for the product to egress from the container. Closing the valve terminates flow of product and movement of piston.

CLAIMS

1. A valved pressure container having an aqueous saline solution under superatmospheric pressure stored therein, said saline solution having been subjected to electrolytic action to effect a sterilization of the saline solution and consequent sterilization of inner surfaces of the container and any other products stored within the container.
- 5 2. A container according to claim 1, wherein the saline solution is subjected to electrolytic action prior to being disposed within the container.
- 10 3. A container according to either of claims 1 and 2, wherein the saline solution is an isotonic saline solution.
- 15 4. A container according to any preceding claim, wherein the saline solution has been subjected to sufficient electrolysis that the saline solution has a bactericidal/bacteriostatic activity for a protracted period.
- 20 5. A container according to any preceding claim, wherein the superatmospheric pressure is generated by a pressure generating propellant.
6. A container according to claim 5, wherein the saline solution is in contact with the pressure generating propellant.
- 25 7. A container according to any one of claims 1 to 5, comprising an aerosol container wherein the superatmospheric pressure is generated by disposing the saline solution on a valved side of a piston disposed within the aerosol container and by disposing a pressure generating propellant on a non-valved side of the piston.
- 30 8. A method for sterilizing an aerosol container comprising sealing in the container under superatmospheric pressure a saline solution that has been subjected to electrolytic action.
- 35 9. A method according to claim 8, wherein the saline solution is electrolyzed prior to being disposed in the aerosol container.

10. A method according to either of claims 8 and 9, wherein the saline solution is an isotonic saline solution.
11. A method according to any one of claims 8 to 10, wherein the saline solution is subjected to sufficient electrolytic action so as to impart bactericidal/bacteriostatic activity to the saline solution for a protracted period.
5